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| 10/564,284 | 03/14/2006 | Irene Tatschett | 0512-1317 | 7547 |
| <div>466 7590 07/02/2009</div> <div>YOUNG & THOMPSON 209 Madison Street Suite 500 ALEXANDRIA, VA 22314</div> | | | | |
| EXAMINER | | | | |
| O HARA, EILEEN B | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/564,284

Applicant(s)

TATISCHEFF ET AL.

Examiner

EILEEN B. O HARA

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-14 is/are pending in the application.
- 4a) Of the above claim(s) 13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11 and 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-893)
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date 1/11/06

DETAILED ACTION

Change of Examiner and Art Unit

The Examiner and Art Unit of your application in the PTO have changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Eileen O'Hara in Art Unit 1638.

Status of Claims

Claims 11-19 are pending in the instant application. Claims 15-19 have been canceled as requested by Applicant in the Paper filed July 21, 2008.

This is the First Office Action on the Merits of US Application 10/564,284, filed 14 March 2006, which is a National Stage continuation of PCT/IB04/02265, filed 13 July 2004, which claims Foreign priority to EPO 03291752.8, filed 15 July 2003.

Election/Restrictions

Applicant's election with partial traverse of Group I (Claims 11-12) in the reply filed on 21 July 2008 is acknowledged. The traversal is on the ground(s) that Applicant states that Groups I and II should be rejoined because Applicant states that "both Groups I and II require the special technical feature of a molecule of interest different from Hoeschst 33342 in the vesicles, said molecule of interest allowing the therapeutic or diagnostic use of the vesicle". In addition, Applicants recite that "The Official Action does not appear to dispute this, but rather seems not to have recognized this feature and rather focuses on another recitation which the Official Action states is not patentable". Furthermore, Applicants disagree that the Tatischeff et al reference is

prior art and submit that "the vesicles prepared in the absence of Hoechst 33342 do not contain a molecule of interest", said molecule of interest "allowing the therapeutic or diagnostic use of the vesicle". In addition, Applicants traverse that Groups I and II should be rejoined because Applicants state that the vesicles of Claims 13-14 are necessarily made by the process of claims 11-12 and that conversely, the process of claims 11-12 necessarily lead to the preparation of the vesicle claimed in claims 13-14.

Applicants traverse is respectfully not found persuasive because firstly, Applicants arguments are not commensurate with the scope of the claims because the claims do not recite that said molecule of interest is for allowing "the therapeutic or diagnostic use of the vesicle", and secondly, because the previous Office Action *does* recognize the claimed feature of a molecule of interest different from Hoeschst 33342, stating "Tatischeff et al. also disclose that the vesicles contain DNA molecules of interest and disclose that the method of making the vesicles includes culturing cells both in the presence and absence of the Hoechst 33342 and explicitly contemplate producing the vesicles in the absence of the Hoechst 33342 (page 484-485, paragraph bridging pages). Therefore, claims 11-12 lack a special technical feature and cannot share one with claims 12-13 and hence there is no unity of invention.

In addition, Applicants traverse that Groups I and II should be rejoined because Applicants state that the vesicles of Claims 13-14 *are necessarily* made by the process of claims 11-12 is respectfully not found persuasive because the vesicles of Claims 13-14 do not depend from Claims 11 or 12.

The requirement is still deemed proper and is therefore made FINAL.

Claim 13 and 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 21, 2008.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on January 11, 2006 is in compliance with the provisions of 37 CFR 1.97, except for Tatischeff et al., which is missing page 477 of the paper. The Examiner has provided a complete copy of the Tatischeff et al. reference with the present office action. Accordingly, the IDS has been considered by the examiner.

Specification

The disclosure is objected to because of the following informalities:

The application appears to be a translation of a foreign application and has numerous grammatical and other errors. For example on page 1, line 10, "of" should be "on", on page 2 line 4, "insight in" should be "insight into", at line 26, "chock" should be "shock", on page 29, line 8, "synthesized" should be "synthesize", on page 22 line 10 and on page 30 line 2, "35-30" should be "30-35", on page 30 line 9, "either" should be deleted, on page 31, line 7, "to" should be "with" and on page 33, line 3, "sensible" should be "sensitive".

On page 14, line 26, LUV should also be described as "large unilaminar vesicles" for clarity.

Appropriate correction is required.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 recites that the vesicle is not a *Dictyostelium discoideum* vesicle, but claim 12 recites that the vesicle is a *Dictyostelium discoideum* vesicle.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite because as written at the end of the claims:

“with the proviso that said vesicle is not a *Dictyostelium discoideum* vesicle containing Hoechst 33342.”

It is not clear if the vesicle is not a *Dictyostelium discoideum* vesicle that **may** contain Hoechst 33342, or if the vesicle is not a *Dictyostelium discoideum* vesicle that **may not** contain Hoechst 33342.

Claim 12 is indefinite because it is a dependent claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tatischeff et al., CMLS Cellular and Molecular Life Sciences, Vol. 54, pages 475-487, 1998.

Claim 12 is drawn to a method for preparing a non-pathogenic amoeba vesicle that contains a molecule of interest, wherein the amoeba is *Dictyostelium discoideum*, with the proviso that said vesicle is not a vesicle containing Hoechst 33342.

Tatischeff et al. disclosed a method of culturing *Dictyostelium discoideum* cells with Hoechst 33342 dye to make vesicles from that contain the Hoechst 33342 dye. Tatischeff et al. did not culture the *Dictyostelium discoideum* cells with any other molecule. However, Tatischeff et al. did teach that in order to determine if other xenobiotics could be detoxified by the mechanism of extra-cellular shedding of vesicles, experiments should be carried out with anthracyclines and other cytotoxic drugs (see page 485-486 and below).

The present observation of a cellular traffic targeting HC342 into the extracellular medium by means of vesicles indicates a new possible mechanism for the high cellular resistance of *Dd* cells against this DNA-targeted vital stain. However, before being able to extend such a mechanism mediated by vesicular traffic to detoxification of other xenobiotics, experiments should be carried out with anthracyclines and other cytotoxic drugs binding to targets other than nucleic acids.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing the application, to culture *Dictyostelium discoideum* cells with anthracyclines and other

cytotoxic drugs, in order to determine if such compounds would be enclosed in vesicles that would then be shed into the extra-cellular medium. The motivation to do so comes from Tatischeff et al., who expressly state that such experiments should be done. There would be a reasonable expectation of success, since the Hoechst 33342 dye was taken up and then shed in vesicles.

Further, the Supreme Court has determined, in *KSR International Co. v. Teleflex, Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007), that “a person of ordinary skill attempting to solve a problem will” not “be led only to those elements of prior art designed to solve the same problem.....” (KSR, 550 U.S. at ___, 82 USPQ2d at 1397). In addition, the court found that “When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variant, 35 USC 103 likely bars its patentability” (KSR, 550 U.S. at ___, 82 USPQ2d at 1396). Further the court found that the Federal Circuit has erred in applying the teaching-suggestion-motivation test in an overly rigid and formalistic way, in particular by concluding “that a patent claim cannot be proved obvious merely by showing that the combination of elements was ‘obvious to try’” (KSR, 550 U.S. at ___, 82 USPQ2d at 1397) and has further determined that “.....[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results” (KSR, 550 U.S. at ___, 82 USPQ2d at 1395). The court further found that “..... the conclusion that when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious” (KSR, 550 U.S. at ___, 82 USPQ2d at 1395-1396). Thus, when considering obviousness of a combination of known elements, the operative question is “whether the improvement is more than the predictable use of prior art elements according to their established functions” ((KSR, 550 U.S. at ___, 82 USPQ2d at 1396).

Given the above, applying the same logic to the instant process claims, it would have been *prima facie* obvious to modify the method of Tatischeff et al. to produce the instantly claimed method because Tatischeff et al. specifically recognized the problem or need in the art to solve the problem of determining if cells that are resistant to other xenobiotics are resistant using the method of shedding vesicles containing the xenobiotics.

Further, given the known problem to be solved, given the known conventional and successful techniques for solving the problem, given that Tatischeff et al. provides a specific identified, predictable, potential solution to the recognized problem, the variation of the technique of Tatischeff et al. et al is obvious.

Finally, given the above, the claimed invention is obvious over the prior art because it would have been obvious to try the known methods suggested by Tatischeff et al. for the determination of drug resistance was mediated by vesicle shedding.

Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tatischeff et al., CMLS Cellular and Molecular Life Sciences, Vol. 54, pages 475-487, 1998, and further in view of "The Cellular Slime Molds", John Tyler Bonner, second edition 1967.

Claim 11 is drawn to a method for preparing a non-pathogenic amoeba vesicle that contains a molecule of interest, wherein the amoeba is not *Dictyostelium discoideum*, with the proviso that said vesicle is not a vesicle containing Hoechst 33342.

Bonner teaches that *Dictyostelium discoideum* as well as *Dictyostelium lacteum*, *Dictyostelium minutum*, *Dictyostelium mucoroides*, and *Dictyostelium purpurem* are all slime molds that exist as single cells, but can aggregate and form fruiting bodies (pages 34-44).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing the application, to culture any of the *Dictyostelium* species taught in Bonner cells with either a vital dye such as Hoechst 33342, anthracyclines and other cytotoxic drugs, in order to determine if such compounds would be enclosed in vesicles that would then be shed into the extra-cellular medium. One of ordinary skill in the art would be motivated to do so, in order to determine if the other *Dictyostelium* species had the same kind of mechanism. There would be a reasonable expectation of success, since the Hoechst 33342 dye was taken up and then shed in vesicles in *Dictyostelium discoideum*, and the other species appear to be closely related.

Further, the Supreme Court has determined, in *KSR International Co. v. Teleflex, Inc.*, 550 U.S., 82, USPQ2d 1385 (2007), that "a person of ordinary skill attempting to solve a problem will" not "be led only to those elements of prior art designed to solve the same

problem.....” (KSR, 550 U.S. at_, 82 USPQ2d at 1397). In addition, the court found that “When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variant, 35 USC 103 likely bars its patentability” (KSR, 550 U.S. at_, 82 USPQ2d at 1396). Further the court found that the Federal Circuit has erred in applying the teaching-suggestion-motivation test in an overly rigid and formalistic way, in particular by concluding “that a patent claim cannot be proved obvious merely by showing that the combination of elements was ‘obvious to try’” (KSR, 550 U.S. at_, 82 USPQ2d at 1397) and has further determined that “.....[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results” (KSR, 550 U.S. at_, 82 USPQ2d at 1395). The court further found that “..... the conclusion that when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious” (KSR, 550 U.S. at_, 82 USPQ2d at 1395-1396). Thus, when considering obviousness of a combination of known elements, the operative question is “whether the improvement is more than the predictable use of prior art elements according to their established functions” ((KSR, 550 U.S. at_, 82 USPQ2d at 1396).

Given the above, applying the same logic to the instant process claims, it would have been *prima facie* obvious to modify the method of Tatiseff et al. to produce the instantly claimed method because Tatiseff et al. discovered that *Dictyostelium discoideum* shed vesicles containing Hoechst 33342.

Pertinent Art

The art considered pertinent to the present application is Tatiseff et al., Journal of Fluorescence, Vol. 18, pages 310-328, 2008, which discloses experiments in which Hoechst 33342 loaded into *Dictyostelium discoideum* vesicles is transferred into naïve *Dictyostelium discoideum* cells as well as human leukemia cells. This is not considered prior art, but is cited as of interest in the present application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara whose telephone number is (571) 272-0878. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://portal.uspto.gov/external/portal/pair>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eileen B. O'Hara/
Primary Examiner
Art Unit 1638